The Kinetics of the Reactions of Picryl Chloride with Some Substituted Anilines. Part 5 [1]

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Arrhenius parameters have been measured for the reactions of picryl chloride with the following substituted anilines in acetonitrile: 3-amino- and 3-methyl-aniline, 3-amino-5-nitroaniline, 3-fluoro-5-methylsulphonylaniline, 3-X-5-methylanilines (X = NO_2, OMe, CH_3, F, Cl, Br, or I) and 3,5-X_2-anilines (X = F, Cl, Br, or I). A total of 33 3,5-disubstituted anilines have now been examined for the additivity of substituent effects on the free energy of activation, and it has been shown that with the exception of 3-amino-5-nitroaniline this hypothesis reproduces experimental rate constants within a factor of 2. A rationalization is proposed for the deviations that occur in some cases when more stringent criteria of additivity are used.

We have examined the additivity of substituent effects in the reactions of 3,5-disubstituted anilines with picryl chloride in acetonitrile. We have now extended our investigations to the series 3-X-5-methylanilines (X = NO_2, OMe, CH_3, F, Cl, Br, or I), 3,5-X_2-anilines (X = F, Cl, Br, or I), and, to complete earlier series,[1] 3-fluoro-5-methylsulphonyl- and 3-amino-5-nitro-aniline. The Arrhenius parameters for the reactions of 3-methyl- and 3-amino-anilines with picryl chloride in acetonitrile have also been determined and the rate constants for the reactions of all four 3-halogenobenzenes have been measured directly at 25 °C to reduce errors in the calculation of the additivity of substituents effects. The reactions were followed by the spectrophotomeric estimation of the products, with the amines in large enough excess to give first-order kinetics, and in all cases optical densities at infinity agreed with the theoretical ones. Values of the Arrhenius parameters and rate constants at 25 °C are given in Table 1.

TABLE 1

Rate constants (l mol^{-1} s^{-1}) measured directly at 25 °C and Arrhenius parameters for the reactions of picryl chloride with some substituted anilines in acetonitrile

Substituent	10^5k [a]	E/kcal mol^{-1}	log A
3-NH_2 [b]	$3.91 \pm 0.01 \times 10^4$	7.5 ± 0.14	5.11
3-Me	$2.88 \pm 0.02 \times 10^4$	7.5 ± 0.04	4.96
3-F	$7.48 \pm 0.03 \times 10^2$		
3-Cl	$6.34 \pm 0.04 \times 10^2$		
3-Br	$6.65 \pm 0.03 \times 10^2$		
3-I	$1.34 \pm 0.01 \times 10^3$		
3,5-Me_2	$4.14 \pm 0.01 \times 10^4$	7.5 ± 0.13	5.11
3-NO_2,5-Me	$8.00 \pm 0.02 \times 10$	10.5 ± 0.12	4.60
3-OMe,5-Me	$1.24 \pm 0.05 \times 10^4$	8.4 ± 0.06	5.21
3-F,5-Me	$1.06 \pm 0.03 \times 10^3$	9.8 ± 0.09	5.21
3-Cl,5-Me	$8.31 \pm 0.09 \times 10^2$	10.1 ± 0.11	5.32
3-Br,5-Me	$9.43 \pm 0.04 \times 10^2$	9.7 ± 0.04	5.09
3-I,5-Me	$1.95 \pm 0.06 \times 10^3$	9.1 ± 0.11	4.96
3,5-F_2	$2.74 \pm 0.02 \times 10$	11.0 ± 0.08	4.49
3,5-Cl_2	$2.15 \pm 0.06 \times 10$	11.3 ± 0.04	4.58
3,5-Br_2	$2.49 \pm 0.02 \times 10$	11.3 ± 0.08	4.68
3,5-I_2	$9.04 \pm 0.05 \times 10$	10.7 ± 0.1	4.80
3-F,5-SO_2Me	5.21 ± 1.93 [c]	12.1 ± 0.22	4.59
3-NH_2,5-NO_2 [b]	$3.91 \pm 0.07 \times 10^2$	9.9 ± 0.03	4.85
H	$2.04 \pm 0.01 \times 10^4$ [d]		

[a] The errors quoted are standard errors of the mean. [b] All values quoted for 3-amino- and 3-amino-5-nitroanilines are statistically corrected for the presence of two amino-groups. [c] Calculated from the Arrhenius parameters. [d] Value from ref. 4.

The introduction of a 3-methyl group into aniline increases the rate constant for the reaction by a factor of 1.4 and the introduction of a second methyl group in the 5-position gives a further 1.4-fold increase. A 3-amino-group is also mildly activating, increasing the rate constant by a factor of 1.9. Similarly a comparison of the results for 3-amino-5-nitroaniline with those for 3-nitroaniline given in Part 3 [2] shows that the introduction of a 5-amino-group into the 3-nitroaniline series increases the rate-constant by a factor of 6.9. Hence the overall effect of a *meta*-amino-group is an electron-releasing one when it is present in either the nucleophile or the substrate of aromatic nucleophilic substitution reactions, as Bevan, Hirst, and Una [3] have shown that in the methoxydefluorination of substituted 3-nitrofluorobenzenes, a 5-amino-group is deactivating. In this respect it differs from the *meta*-methoxy-group, which we have shown has a net electron withdrawing effect when present in the nucleophile,[1] but is electron releasing when present in the substrate.[3] Given the relative magnitudes of the $-I$ and $+M$ effects of the amino- and methoxy-groups, the results are intelligible if, as we have suggested previously,[4] aromatic nucleophilic substitution reactions are more sensitive to the electronic effects of *meta*-substituents, particularly their $+M$ effects, when the substituent is in the substrate rather than in the nucleophile.

A comparison of the present results with those for 3-halogenoanilines [2] shows that the introduction of a 5-methyl group increases the rate constant approximately 1.4 fold. The reactivity sequence I > F > Br > Cl remains constant in the range 0—100 °C, but the span encompassed is small and never exceeds a factor of 2. The magnitude of log A increases with increase in activation energy, a feature which is general for all the 3-halogeno-5-X-anilines series (X $\neq$ halogen) we have investigated, although the sequences (*e.g.* log A, Cl > F > Br > I, for X = Me) are not the same in all series.

The same sequence of rate constants is obtained for the dihalogenoaniline series at 0 °C as for the methyl series, although the spread of reactivities is somewhat greater as there is a factor of 5 between the lowest and highest values. As the temperature increases, this factor decreases, becoming 3.8 at 100 °C, and the reactivity

TABLE 2

A comparison of experimentally determined rate constants, k_m (l mol^{-1} s^{-1}), with those calculated on the assumption of additivity, $k_{calc.}$,* for the reactions of 3,5-disubstituted anilines with picryl chloride in acetonitrile at 25 °C

$-I -K$: $-I -K$

Groups	$10^6 k_{calc.}$	$10^6 k_m$
CF_3/CF_3	33.1 ± 0.7	26 ± 6
SO_2Me/SO_2Me	9.34 ± 0.11	12 ± 2.5
NO_2/NO_2	1.59 ± 0.02	1.00 ± 0.3
CF_3/NO_2	7.25 ± 0.13	6.76 ± 0.44
NO_2/SO_2Me	3.85 ± 0.04	1.62 ± 0.16

$-I -K$: $-I + K$

Groups	$10^5 k_{calc.}$	$10^5 k_m$
NO_2/F	2.09 ± 0.02	1.46 ± 0.17
NO_2/Cl	1.77 ± 0.02	2.38 ± 0.28
$NO_2/Br\cdot$	1.85 ± 0.02	1.95 ± 0.10
NO_2/I	3.74 ± 0.04	2.22 ± 0.30
$MeSO_2/F$	5.06 ± 0.05	5.21 ± 1.93
$MeSO_2/Cl$	4.29 ± 0.05	5.08 ± 0.86
$MeSO_2/Br$	4.50 ± 0.04	4.29 ± 0.47
$MeSO_2/I$	9.06 ± 0.10	9.53 ± 0.27
NO_2/OMe	24.8 ± 0.3	24.7 ± 3.8
CF_3/OMe	113 ± 2	151 ± 2
$MeSO_2/OMe$	60.2 ± 0.7	73.7 ± 0.6
NO_2/NH_2	109 ± 1	391 ± 7

$-I +K$: $-I + K$

Groups	$10^5 k_{calc.}$	$10^5 k_m$
OMe/F	326 ± 3	423 ± 11
OMe/Cl·	276 ± 3	296 ± 1
OMe/Br·	290 ± 3	301 ± 3
OMe/I	584 ± 7	473 ± 3
OMe/OMe	$3\,880 \pm 53$	$5\,080 \pm 60$
F/F	27.4 ± 0.2	27.4 ± 0.2
Cl/Cl	19.7 ± 0.2	21.5 ± 0.6
Br/Br	21.7 ± 0.2	24.9 ± 0.2
I/I	88.0 ± 1.0	90.4 ± 0.5

$+I$: $+I$ or $\pm I$: $- I \pm K$

Groups	$10^4 k_{calc.}$	$10^4 k_m$
Me/Me	$4.07 \pm 0.04 \times 10^3$	$4.14 \pm 0.01 \times 10^3$
Me/NO_2	8.03 ± 0.09	8.00 ± 0.02
Me/OMe	$1.26 \pm 0.02 \times 10^3$	$1.24 \pm 0.05 \times 10^3$
Me/F	106 ± 1	106 ± 3
Me/Cl	89.5 ± 1	83.1 ± 1
Me/Br	93.9 ± 0.9	94.3 ± 0.4
Me/I	189 ± 2	195 ± 6

*All values have been recalculated using values for the rate constants of the 3-substituted anilines measured directly at 25 °C.

sequence changes to I > Br ~ F > Cl. For the same reactions in methanol,[5] rate constants, activation energies, and frequency factors are greater in this solvent than in acetonitrile.

These two series conclude our investigation of the additivity of substituent effects from the 3,5-positions. The results for the 33 disubstituted compounds examined are assembled in Table 2 where the substituents are arranged according to Ingold's classification of electronic effects. The most outstanding feature of the results is the extent of the agreement with the additivity principle. The nucleophiles investigated (including the monosubstituted series) have a range of reactivity of *ca.* 400 000, yet the assumption of the additivity of the free energies of activation reproduces the rate constants to within a factor of 2, except for the couple NH_2/NO_2, the combination of the most activating and deactivating groups.

As discussed earlier,[4] because of the wide range of reactivities involved, for a more precise examination of substituent effects we have adopted the procedure of calculating the rate constant for the disubstituted compound and its statistical error at 25 °C, assuming the additivity of the free energies of activation, and comparing this with the value of the rate constant and its statistical error obtained either by direct measurement at 25 °C or calculated from the experimentally determined Arrhenius parameters of the reaction. We now use the criterion that if the two results agree within three standard deviations, the effects are said to be additive. As a result of this procedure a few combinations of substituent effects are classified as additive because, due to experimental difficulties, there are relatively large errors in the values of the measured rate constants for the disubstituted compounds, and it is possible that if more accurate values could be obtained the effects would be found to be non-additive.* On the basis of this criteria the following combination of groups have substituent effects which are not additive: $NO_2/SO_2Me(-)$;† $NO_2/F(-)$; $NO_2/I(-)$; $OMe/CF_3(+)$; $OMe/SO_2Me(+)$; OMe/F(+); OMe/Cl(+); OMe/I(−); OMe/OMe(+); $NH_2/NO_2(+)$; Br/Br(+).

Before examining possible reasons for departure from additivity in terms of the electronic effects of the substituents, it is as well to stress that for unsymmetrical disubstituted compounds to exhibit additivity not only must changes in potential energy between initial and transitions states due to the substituents be additive, but the differences in solvation energy of the states must either be the same for the unsubstituted, two monosubstituted, and the disubstituted compounds or they must be additive. Hence deviations from additivity could arise from environmental effects and conversely occasionally observed additivity could be due to a fortuitous compensation of internal and external factors. In view of these uncertainties it is prudent to look for broad patterns which are susceptible to theoretical interpretations rather than account for each individual case.

In electrophilic aromatic substitution, Richards, Wilkinson, and Wright [6] have explained deviations from additivity in terms of a demand-dependent free-energy relationship. This predicts lower rates than those expected by application of the additivity principle except where one substituent activates and the other deactivates. Similarly Ridd *et al.*[7] have explained their observations on the deviation from additivity in brominations and nitrations by assuming that the introduction of strong deactivating groups moved the transition state slightly along the reaction co-ordinate towards the Wheland intermediate, making it more sensitive to substituent effects. The positive deviations observed with two

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* In the many cases where it has been possible to measure the rate constant for the disubstituted substrate directly at 25 °C the simple assumption that there is additivity if there is agreement to within ±5% between measured and calculated values leads to the same conclusions.

† Signs refer to those of $k_{obs.} - k_{calc.}$.

weakly deactivating groups $[CH_2]_2\overset{+}{N}Me_3$ and $[CH_2]_2\overset{+}{S}Me_2$ were explained by a special effect based on the conformations available to these groups which cannot be applied in the present case.

In applying the above concepts to the results reported herein, it must be emphasised that if the overall electronic effect of a group X is assessed by the k_X/k_H ratio, then with the exception of the 3-amino- and 3-methyl-groups all the substituents examined in this study are deactivating. On this basis the direction of the deviations from additivity for combinations involving the nitro-group are in agreement with the concepts, but those involving the methoxy-group (with the exception of MeO/I) and the 3,5-dibromo-combination are not.

The overall electronic effect of a methoxy-group is a combination of its $-I$ and $+K$ effects and depends on the position of the group in the aromatic ring with respect to the reaction centre and also the sensitivity of the reaction to inductive and conjugative effects. Thus as we have mentioned earlier a 3-methoxy-group is deactivating when present in both the substrate and nucleophile of nucleophilic aromatic substitutions. In electrophilic aromatic substitution its strong activation of the 2- and 4-positions has been ascribed to a powerful $+E$ effect. Applied to the present results this interpretation implies that as the introduction of deactivating groups into the aniline molecule leads to progressively later transition states, electron release from the methoxy-group increases, leading to positive deviations from additivity. A similar explanation can be put forward for the behaviour of other $-I + K$ groups and it is interesting to note that the mildly deactivating groups that Ridd *et al.* observed to give positive deviations from additivity are also *ortho–para* directing.

EXPERIMENTAL

Materials.—The purification of commercial samples of 3-fluoro-, 3-chloro-, 3-bromo-, and 3-iodo-aniline and the preparation of picryl chloride have been described previously [2] and the preparation and purification of the 3,5-dihalogenoanilines was given in Part 2 of this series.[5] 3-Methyl-, b.p. 203 °C, and 3,5-dimethyl-aniline, b.p. 99—100 °C at 20 mmHg, were commercial samples purified by fractionation and their purity was confirmed by g.l.c. The fraction of 3-aminoaniline, b.p. 280—284 °C, was recrystallised from water, m.p. 63 °C (lit.,[8] 63 °C).

3-*Methyl*-5-*nitroaniline.*—4-Methylaniline was acetylated, dinitrated, hydrolysed, and deaminated by standard methods to give 3,5-dinitrotoluene. Selective reduction with ammonium polysulphide gave 3-methyl-5-nitroaniline, m.p. 97—98 °C (lit.,[9] 98 °C).

3-*Fluoro*-5-*methylaniline.*—3-Methyl-5-nitroaniline was converted *via* the diazonium fluoroborate into 3-fluoro-5-methylnitrobenzene, m.p. 40 °C (lit.,[10] 40—40.5 °C). Reduction with stannous chloride and hydrochloric acid gave 3-fluoro-5-methylaniline.

3-*Chloro*-5-*methylaniline.*— 3-Chloro-5-methylnitrobenzene, m.p. 60 °C, obtained from 3-methyl-5-nitroaniline, by the Sandmeyer reaction, on reduction with stannous chloride and hydrochloric acid gave 3-chloro-5-methylaniline, b.p. 248 °C at 750 mmHg (lit.,[11] 242 °C at 730 mmHg).

3-*Bromo*-5-*methylaniline.*— 3-Bromo-5-methylnitrobenzene obtained from 3-methyl-5-nitroaniline by the Sandmeyer reaction, on reduction with stannous chloride and hydrochloric acid, gave the required amine, m.p. 34—35 °C (lit.,[12] 36 °C).

3-*Iodo*-5-*methylaniline.*—Addition of potassium iodide to a solution of diazotised 3-methyl-5-nitroaniline gave 3-iodo-5-methylnitrobenzene, m.p. 103 °C (lit.,[13] 103—105 °C). Reduction with stannous chloride and hydrochloric acid gave 3-iodo-5-methylaniline, m.p. 76—78 °C (lit.,[13] 78.5 °C).

3-*Fluoro*-5-*methylsulphonylaniline.*—This compound was prepared by the method of Ephraim-Bassey, Emokpae, and Hirst,[14] m.p. 117 °C (lit.,[14] 117—118 °C).

3-*Methoxy*-5-*methylaniline.*—A mixture of 3-fluoro-5-methylnitrobenzene (0.3 mol), sodium methoxide (0.4 mol), and dry methanol was heated in a sealed tube at 130 °C for 10 h. The light yellow precipitate of 3-methoxy-5-methylnitrobenzene obtained on cooling and neutralisation of the mixture with concentrated hydrochloric acid was filtered off, washed with water, and recrystallised from light petroleum (b.p. 60—80 °C), m.p. 70—71 °C (lit.,[15] 70 °C). Reduction with stannous chloride and hydrochloric acid gave 3-methoxy-5-methylaniline, m.p. 48 °C (lit.,[15] 46—47 °C).

3-*Amino*-5-*nitroaniline.*—3,5-Dinitroaniline obtained from 3,5-dinitrobenzoic acid by Schmidt's reaction was selectively reduced by Idoux's method to give 3-amino-5-nitroaniline, m.p. 140 °C (lit.,[16] 141 °C).

Kinetic Measurements.—Details of the method of purification of acetonitrile and the procedure for following the reactions by the spectrophotometric estimation of the products have been given elsewhere.[4] The initial concentrations of picryl chloride and the amines were 1.00×10^{-3}M and 1.00×10^{-2}M except for the fast reactions of 3-methyl-, 3,5-dimethyl-, and 3-amino-aniline when these concentrations were reduced by a factor of 10. The results at various temperatures are listed in Supplementary Publication No. SUP 22680 (3 pp.).*

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* For details of the Supplementary Publications scheme see Notice to Authors No. 7, *J.C.S. Perkin II*, 1979, Index Issue.

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